Heterogeneous endosomal dynamics within eukaryotic cells

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Transport processes of many organelles inside living cells display anomalous diffusion defined by the non-linear growth of the mean squared displacement. This means that the movement of these organelles deviates from Brownian diffusion, but rather they move in a complicated manner. One such organelle is endosomes in eukaryotic cells. Endosomes play an essential role in the transport of molecules such as proteins and lipids within cells. However, the transport of these structures is not uniform, and they are heterogeneous in space and time. In eukaryotic cells, endosomes form a highly dynamic and heterogeneous network which is comprised of various forms of early and late endosomes, each with distinct structures and functions1. The endosomal network plays a major role in sorting and transporting proteins and lipids that are taken in from the cell surface and need to be delivered to lysosomes for degradation. Early endosomes, formed by the budding of clathrin-coated vesicles, are characterized by their high levels of Rab5, a small GTPase protein. Late endosomes, on the other hand, are characterized by lower levels of Rab5 and higher levels of Rab72. Rab5 early endosomes move towards the cell nucleus via dynein3, fuse with one another, increasing in size, and change in membrane composition. The open question remains: how does the heterogeneity of the endosomal network influence endosomal dynamics? To understand the complexity of endosomal transport, large ensembles of single particle trajectories are studied. These ensembles allow the heterogeneities to be quantified in detail and provide insights for mathematical modelling. Accurate mathematical models for heterogeneous dynamics have the potential to enable the design and optimization of various technological applications, such as the design of effective drug delivery systems. The central questions in the analysis of anomalous dynamics are ergodicity and statistical ageing. Ergodicity means that a system will eventually explore all possible states, whereas statistical ageing means that the dynamics of a system change over time. These two concepts are important in selecting the proper model for the description of anomalous dynamics. It is believed that non-ergodicity and ageing come together, but this is not always the case. Endosomal transport is paradoxical since it is ergodic but shows ageing. This behaviour is caused by ensemble heterogeneity, which is an inherent property of endosomal motion. In addition to space-time heterogeneity within a single trajectory, there is heterogeneity across the ensemble of endosomes. The discovery of the paradoxical behaviour of endosomal transport introduces novel approaches for the analysis and modelling of heterogeneous dynamics. These approaches can be used to develop more accurate mathematical models that can help design and optimize technological applications, such as drug delivery systems. The study of endosomal transport provides valuable insights into the complexities of transport processes within living cells. By understanding the heterogeneities of transport processes and developing accurate mathematical models, we can design and optimize technological applications that can greatly benefit human health.